

1. AMENDMENT

1.1 IN THE SPECIFICATION:

Please replace paragraph 10 at pages 5 and 6, line 5, with the following amended paragraph:

The compound is preferably an antagonist of C5a receptors on human and mammalian cells including, but not limited to, human polymorphonuclear leukocytes and human macrophages. The compound preferably binds potently and selectively to C5a receptors, and more preferably has potent antagonist activity at sub-micromolar concentrations. Even more preferably the compound has a receptor affinity $IC_{50} < 25 \mu M$, and an antagonist potency $IC_{50} < 1 \mu M$.

Please replace paragraph 2 at page 9, line 12, with the following amended paragraph:

An "uncommon" amino acid includes, but is not restricted to, D-amino acids, homo-amino acids, N-alkyl amino acids, dehydroamino acids, aromatic amino acids other than phenylalanine, tyrosine and tryptophan, ortho-, meta- or para-aminobenzoic acid, ornithine, citrulline, canavanine, norleucine, ~~γ-glutamic~~ glutamic acid, aminobutyric acid, L-fluorenylalanine, L-3-benzothierylalanine, and α, α -disubstituted amino acids.

Please replace paragraph 4 at page 13, lines 20 and 24 with the following amended paragraph:

Assays were performed with fresh human PMNs, isolated as previously described (Sanderson *et al*, 1995), using a buffer of 50 mM HEPES, 1 mM $CaCl_2$, 5 mM $MgCl_2$, 0.5%

bovine serum albumin, 0.1% bacitracin and 100 μ M phenylmethylsulfonyl fluoride (PMSF). In assays performed at ~~4 \pm 4~~ 4 $^{\circ}$ C, buffer, unlabelled human recombinant C5a (Sigma) or peptide, Hunter/Bolton labelled 125 I-C5a (\sim 20 pM) (New England Nuclear, MA) and PMNs (0.2×10^6) were added sequentially to a Millipore Multiscreen assay plate (HV 0.45) having a final volume of 200 μ L/well. After incubation for 60 min at ~~4 \pm 4~~ 4 $^{\circ}$ C, the samples were filtered and the plate washed once with buffer. Filters were dried, punched and counted in an LKB gamma counter. Non-specific binding was assessed by the inclusion of 1mM peptide or 100 nM C5a, which typically resulted in 10-15% total binding.

Please replace paragraph 6 at page 13 at line 31, and page 14, at line 1 with the following amended paragraph:

Cells were isolated as previously described (Sanderson *et al*, 1995) and incubated with cytochalasin B (5 μ g/mL, 15 min, ~~37 \pm 3~~ 37 $^{\circ}$ C). Hank's Balanced Salt solution containing 0.15% gelatin and peptide was added on to a 96 well plate (total volume 100 μ L/well), followed by 25 μ L cells (4×10^6 /mL). To assess the capacity of each peptide to antagonise C5a, cells were incubated for 5 min at ~~37 \pm 3~~ 37 $^{\circ}$ C with each peptide, followed by addition of C5a (100 nM) and further incubation for 5 min. Then 50 μ L of sodium phosphate (0.1M, pH 6.8) was added to each well, the plate was cooled to room temperature, and 25 μ L of a fresh mixture of equal volumes of dimethoxybenzidine (5.7 mg/mL) and H₂O₂ (0.51%) was added to each well. The reaction was stopped at 10 min by addition of 2% sodium azide. Absorbances were measured at 450 nm in a Bioscan 450 plate reader, corrected for control values (no peptide), and analysed by non-linear regression.

Please replace paragraph 4 at page 17, lines 21 and 23, with the following amended paragraph:

Approximately three weeks after initial clinical signs, the treatment included Clavulox (7 mg/kg administered subcutaneously), doxycycline (5mg/kg administered orally), and enrofloxacin (5mg/kg administered subcutaneously) and terbutaline (0.3 mg/kg administered orally), nebulisation (saline) and percussion, use of Ventolin ~~100~~100µg by puffer inhalation and terbutaline (0.3 mg/kg administered orally) as necessary to control dyspnoea. Prednisolone was given as a single daily dose of 2mg/kg, and Seretide (Salmeterol ~~50~~50µg plus fluticasone ~~250~~250 µg) was given using a mask and spacer. Response to treatment was marked, with improvement in respiratory effort and reduction in crackles audible on auscultation. This combination of treatment was maintained over the next month.

Please replace paragraph 5 at pages 17 and 18, line 2 with the following amended paragraph:

During this month of therapy the following observations were made:

1. There was a radiographic improvement characterised by reduction in the prominence of the bronchointerstitial pattern and reduction in air entrapment.
2. Throughout each day, and from day to day, there was a marked variation in severity of respiratory clinical signs, although these were not as severe as those observed in the initial stages of the disease. Increase in respiratory effort was often observed when the cub was taken into the airconditioned nursery, during exercise or stress, and spontaneously, presumably in response to respiratory irritants in the environment.
3. Respiratory clinical signs responded rapidly to bronchodilators, given either orally terbutaline (0.3 mg/kg orally) or by inhalation (Ventolin puffer ~~100~~100µg).
4. Although response to therapy was marked, there were never times when the breathing pattern was normal.
5. The cub developed a poor “staring” coat, poor muscling, retarded growth rate, reduced activity level and playfulness, and relatively poor appetite when compared with her littermate.

Please replace paragraph 3 at page 18, lines 24 -27 with the following amended paragraph:

Kaasha’s keepers unanimously reported that the breathing pattern improved to virtually normal levels for one week, with no episodes of dyspnoea during that period. However, the clinical pattern of laboured breathing returned to pre-treatment levels at seven to nine days post treatment. At this time therapy included oral corticosteroid at 2mg/kg, use of inhaled Flixotide (Fluticasone ~~250~~250µg/dose) with and without Seretide (Salmeterol

~~50g~~50µg plus fluticasone ~~250g/dose~~250µg/dose), use of Ventolin puffer, ~~100g~~100µg, as necessary to control dyspnoea, and occasional use of Pulmicort nebules (Budesonide ~~400g~~400µg) by nebulisation.

Please replace paragraph 3 at page 19, lines 24 and 25 with the following amended paragraph:

As at July 2002 Kaasha was approximately 32 kg and 7 months of age, and was being maintained on the following regimen:

Macrolone (prednisolone): 20mg orally each evening;

Singulaire (montelukast sodium): 10mg orally each evening;

AcF-[OPdChaWR] (1): 3mg/10kg subcutaneously twice a week;

Seretide puffer (Salmeterol 50µg plus fluticasone 250µg / dose:) morning and night, preceded by Ventolin, 100µg, puffer;

Flixotide puffer (Fluticasone): ~~250g/dose~~250µg/dose up to four times each day; and

Pulmicort nebulisation (Budesonide): ~~400g~~400µg once a day as time permits.